REMARKS

I. Status of the claims

No claims are added, cancelled or amended. Claims 1-47 are pending, claims 9-11, 23, 29 and 44-46 are withdrawn, and therefore claims 1-8, 12-22, 24-28, 30-43, and 47 are under consideration.

II. Finality

Applicants respectfully request reconsideration and withdrawal of the finality of the present Office Action. Both references cited in the Office Action were previously of record in this Application: U.S. Patent No. 5,145,684 (Liversidge) was submitted as reference A4 in the IDS of January 22, 2004; and EP 0 719 549 was cited in the previous Office Action. These references are as relevant to the present claims as they were to those claims previously pending. Therefore, the present rejection could have been asserted by the PTO in the previous round of prosecution. Moreover, the previous amendments to the claims followed from an interview between Applicants' representative and the PTO Examiner and, therefore, the PTO had an opportunity at that time to raise the issues now asserted. Applicants have diligently sought to advance prosecution and believe that it is improper and inequitable for the PTO to now assert this new ground of rejection in a final Office Action.

III. The April 2, 2008 Information Disclosure Statement

The PTO has not indicated that it has considered the IDS filed on April 2, 2008. Applicants respectfully request that the PTO consider the IDS and return an initialed copy of the SB08 in the next communication.

IV. The previous rejections

The PTO has not explicitly indicated the status of the previously pending rejections. As they have not been reasserted, it is assumed that they are overcome.

V. Rejections Under 35 U.S.C. § 103

Claims 1-8, 12-22, 24-28, 30-43 and 47 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over EP 0 719 549 ("EP 549") in view of U.S. Patent No. 5,145,684 to Liversidge *et al.* ("Liversidge"). Applicants respectfully traverse.

A. Comparison between the claimed invention and the cited prior art

As the PTO itself makes clear, "ascertaining the differences between the claimed invention and the prior art requires interpreting the claim language, and considering both the invention and the prior art as a whole." Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in KSR International Co. v. Teleflex Inc. OG Notices: 06 Nov 2007. *See also* MPEP § 2141.02; *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); and *Schenck v. Nortron Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983). Accordingly, the PTO cannot parse out claim limitations and individually evaluate them for obviousness. The proper analysis is why the claim as a whole (considering all the limitations together) is or is not obvious in view of the cited art, as a whole.

B. The claimed invention

Claim 1 is drawn to a solid or semi-solid gelatin pharmaceutical composition comprising:

(a) particles of at least one active agent having an effective average particle size of less than about 2000 nm prior to inclusion in the solid or semi-solid gelatin pharmaceutical composition;

(b) at least one surface stabilizer adsorbed on the surface of the particles; and

(c) a gel matrix of at least one gel forming substance, the gel forming substance in an amount which exhibits gelation sufficient to retain water in an amount of from about 20% to about 97%, based on the total weight of the composition,

wherein nanoparticulate active agent particles with the adsorbed surface stabilizer are dispersed in the gel matrix.

C. EP '549 does not describe the gelatin matrix of the claimed invention

For the PTO's characterization of EP '549, the present Office Action refers to the previous Office Action of October 19, 2007. There, at page 4, the PTO equates the "semi-solid gelatin" of the present invention with the disclosure of EP '549.

> The EP reference teaches compositions of drugs dispersed in gelled agents. . .The compositions are filled in a soft gelatin shell (example 6), which results in a geometric shape, as

> required by instant claim 14, and are understood to include at least one of the gelatin types mentioned in claims 6-8.

As an initial matter, the "soft gelatin shell" of EP '549 does not equate to the gel-matrix of the claimed invention in which the active agent particles are dispersed. Therefore, the comparison must look first to the fill material. EP '549 recites that "[t]he present invention provides a fill material for a soft gelatin capsule comprising a polyalkylene glycol having an average molecular weight of about 600 or less, water and a gelling agent in an amount effective to gel the glycol." *See* EP '549, page 2, "summary of the invention." In the claimed invention, by contrast, none of the gel forming substances recited in claim 8 is a "polyalkylene glycol having a molecular weight of 600 or less." In addition, EP '549 explicitly seeks a translucent gel which is achieved with PEG 400 (*see* EP '549, Examples 2-7), but not other gels, and compositions of higher molecular weight PEG are opaque (*see* Example 1 of EP '549). Therefore, EP '549 is limited to low molecular weight polyalkylene glycols, and teaches away from other gel-forming agents.

Next, the claimed invention seeks to retain water "in an amount of from about 20% to about 97%" as recited in claim 1, which is "essential for effective redispersibility" (paragraph [0018]). By contrast, EP '549 seeks to *minimize* the amount of water. Page 3 of EP '549 recites:

> A *minor proportion of water is also used* in conjunction with the solvent. The gel generally comprises by weight about 35 to about 95 percent solvent and about 5 to about 25 percent water. Unless otherwise stated, the percentages recited herein are by weight of the total weight of the gel fill material, *i.e.*, both the gel and active ingredient.

(*emphasis added*). Because gelatin capsules are water soluble, the use of a fill material with a high water content will degrade the capsule, just as external exposure to water (or even humidity) is deleterious for gelatin capsules. Soft gel capsules have an equilibrium water content of 6-8%. *See, e.g.* www.pformulate.com/labclass/pformsoftgel.cfm, accessed July 3, 2008. Therefore, it is unsurprising that EP '549 would seek to use only a "minor proportion" of water and would teach away from the claimed invention.

Indeed, the person of ordinary skill would question whether EP '549 has enabled the full range of water content it describes. The highest amount of water used in a fill material that was actually loaded into a capsule was 14.6 % (Example 16) and this was in the presence of large amounts of water soluble materials such that the amount of "excess water" may be very low. Crucially for the "pharmaceutical composition" recited in pending claim 1, EP '549 never tests the stability of the capsules to ensure that they do not dissolve shortly after filling, and so there is no reasonable expectation of success even with 14.6% water.

Moreover, there are at least two problems with asserting that the water ranges of EP '549 overlap with that of the claimed invention. Because the gelatin capsule is integral to the composition of EP '549 and to a comparison with the claimed composition, the proper comparison of water content is between the claimed invention and the entire composition of EP '549, which is a filled soft gelatin capsule. Nothing in EP '549 describes the water content of the entire composition, but only that of the *fill material* (EP '549; page 3, lines 8, 12, 19, and 22). Thus, EP '549 does not describe a composition with a water content that overlaps with that of the claimed invention. Second, the person of ordinary skill in the art would not believe that EP '549 is enabled for a range of water content in the fill material (let alone the entire composition) that abuts or overlaps with that of the claimed invention, for reasons described above.

D. EP '549 is restricted to substantially clear filling materials

If active agent nanoparticles were dispersed in a solid gel matrix, as presently claimed, the resulting fill material would be turbid. Turbidity is exactly what EP '549 intends to avoid – "when the fill material of the present invention is introduced into the capsule and gelled, the resulting dosage form has an elegant, translucent or clear appearance." Page 3, lines 27 and 28.

E. Summary

EP '549 fails to teach or enable the claimed gelatin composition. The claimed gelatin composition has an excess water content of no less than 20%, is composed of a class of gelatins, and contains solid particles that impart turbidity. By contrast, EP '549 does not enable materials with a water content of 20% or above; requires that the fill material be a polyalkylene glycol with a molecular weight of 600 or less; and requires that the entire fill

material, including the active ingredients, be substantially translucent or clear in appearance. Thus, EP '549 fails to teach the claimed invention and actually teaches away from the claimed invention in regards to both water content and turbidity. For at least these reasons, EP '549 does not teach or enable the presently claimed invention.

F. Liversidge does not cure the deficiencies of EP '549

For the obviousness rejection to stand, the combination of EP '549 and Liversidge must teach and enable all of the claimed elements. Liversidge is cited for its teaching of nanoparticles with a least one surface stabilizer adsorbed on the surface. It does not cure the multiple deficiencies of EP '549 in respect of water content, fill material or turbidity, and does not remedy the teaching away of EP '549. Accordingly, the claimed invention is not obvious.

These are not the only reasons, however, why the claimed invention is patentable over the combination of EP'549 and Liversidge. For the combination of EP '549 and Liversidge to render obvious the claimed invention, there must be some reason in the art to make the claimed invention and such reason(s) must also account for any teaching away. *See KSR Int'l Co. v. Teleflex, Inc.* 127 S.Ct. 1727, 1731 (2007).

Although Liversidge teaches advantages of 400 nm nanoparticles with a surface stabilizer, no reason is given why this advantage would be useful or practical when placed into the fill material of the soft gelatin capsule of EP '549. There is no teaching that the fill material would have the dispersibility claimed in the present invention, and the resultant improved bioavailability. Indeed, incorporation of the fill material into a gelatin shell only serves to inhibit rapid dispersion. Second, EP '549 explicitly seeks to avoid turbidity, stating 'when the fill material of the present invention is introduced into the capsule and gelled, the resulting dosage form has an elegant, translucent or clear appearance.' EP '549, page 3, lines 27 and 28. The use of the particles of Liversidge would result in a turbid composition, against the explicit teachings of EP '549. Indeed, if one were to seek to obtain a clear gel containing a bioavailable pharmaceutical, one would not seek to use the particles taught by Liversidge, but would seek to first dissolve the active agent in the gel. Thus, there is a very clear reason *against* combining EP '549 and Liversidge in the manner asserted by the PTO.

Accordingly, neither Liversidge nor EP '549, alone or in combination, provide all elements of the claimed invention, the references do not provide a reason to combine the teachings of each to obtain the claimed invention and, in fact, the cited references teach away from the claimed combination. Accordingly, the cited art does not render obvious the claimed invention.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully believe that all rejections have been overcome. Applicants respectfully request that the PTO reconsider and withdraw both the finality of the present Office Action and the present rejections, and allow the pending claims. As Applicants believe that the pending claims are in condition for allowance, Applicants also request that the PTO rejoin and examine the withdrawn claims.

If it is believed that telephone communication can expedite the prosecution of this application, the Examiner is invited to contact the undersigned at the number below.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Simon Elliott
Reg No 54,083

Date July 7, 2008

By _____ for

FOLEY & LARDNER LLP
Customer Number: 31049
Telephone: (202) 672-5538
Facsimile: (202) 672-5399

Michele M. Simkin
Attorney for Applicants
Registration No. 34,717